

MARKED UP COPY OF AMENDMENT

IN THE CLAIMS

Please amend Claims 29, 35-47, 64 and 65 as follows:

--29. (Amended) A method of detecting an endocrine disrupting action of a test substance, comprising:

(A) culturing a cell that is sensitive to an endocrine hormone in the presence of the endocrine hormone and the test substance and detecting a gene expression pattern (1) of said cell; and

(B) culturing said cell that is sensitive to an endocrine hormone in the presence of the endocrine hormone, but in the absence of the test substance, and detecting a gene expression pattern (2) of said cell; and/or

(C) culturing said cell that is sensitive to an endocrine hormone in the absence of the endocrine hormone, but in the presence of the test substance, and detecting a gene expression pattern (3) of said cell; and/or

(D) culturing said cell that is sensitive to an endocrine hormone in the absence of the endocrine hormone and in the absence of the test substance, and detecting a gene expression pattern (4) of said cell; and

(E) comparing gene expression pattern (1) with gene expression pattern (2)[,] and/or (3) and/or (4) to determine the endocrine disrupting activity of the test substance, wherein the increased or decreased expression of a gene in expression pattern (1) compared to the same

gene in expression pattern (2)[,] and/or (3) and/or (4) is indicative of endocrine disrupting action by the test substance.

30. (Unamended) The method of Claim 29, wherein gene expression pattern (1) is compared with gene expression pattern (2).

31. (Unamended) The method of Claim 29, wherein gene expression pattern (1) is compared with gene expression pattern (3).

32. (Unamended) The method of Claim 29, wherein gene expression pattern (1) is compared with gene expression pattern (2) and gene expression pattern (3).

33. (Unamended) The method of Claim 29, comprising comparing gene expression pattern (1) with gene expression pattern (4).

34. (Unamended) The method of Claim 29, wherein said gene expression patterns are measured by determining the variation in the amount of gene transcription.

35. (Amended) The method of Claim 29, comprising recovering RNA corresponding to each gene expression pattern, optionally producing cDNA corresponding to said RNA, and comparing said RNA or cDNA of (A) with that of (B)[,] and/or (C) and/or (D) to determine the endocrine disrupting activity of the test substance, wherein a difference in the amount of RNA or cDNA between (A) and (B), (C) and/or (D) is indicative of the endocrine disrupting activity of the test substance.

36. (Amended) The method of Claim 29, wherein the RNA, or optionally the cDNA corresponding to said RNA, obtained from (A) and (B)[,] and/or (C) and/or (D) is electrophoretically separated to determine the gene expression patterns.

37. (Amended) The method of Claim 35, wherein the RNA, or optionally the cDNA corresponding to said RNA, obtained from (A) is hybridized to the RNA or cDNA obtained

from (B)[,] or (C) or (D), and the gene patterns of (A) and (B)[,] or (C) or (D) are determined after subtraction of the hybridizing RNA or cDNA.

38. (Amended) The method of Claim 29, wherein endocrine disruption is determined by identifying one or more types of RNA expressed in (A), but not expressed in (B)[,] or (C) or (D), or alternatively, one or more types of RNA expressed in (B)[,] or (C) or (D), that are not expressed in (A).

39. (Amended) The method of Claim 29, wherein endocrine disruption is determined by identifying that a different amount of one or more types of RNA is expressed in (A), compared to (B)[,] or (C) or (D).

40. (Amended) The method of Claim 29, comprising:

- (a) recovering RNAs from (A) and (B), and/or (C) and/or (D);
- (b) subjecting the RNAs recovered in step (a) to reverse transcription;
- (c) amplifying reverse transcription products obtained in (b) by PCR; and
- (d) subjecting PCR products obtained in step (c) to electrophoresis, comparing the electrophoretic patterns of bands obtained, thereby detecting a band specific to a first gene expression pattern of (A).

41. (Amended) The method of Claim 29, wherein said gene expression patterns are measured by determining variation in the amount of protein or glycoprotein expression between (A) and (B)[,] and/or (C) and/or (D).

42. (Amended) The method of Claim 29, wherein one or more protein(s) or glycoprotein(s) expressed in (A) and (B)[,] and/or (C) and/or (D) are electrophoretically separated to determine the gene expression patterns.

43. (Amended) The method of Claim 42, wherein the protein(s) or glycoprotein(s) expressed in (A) and (B)[,] and/or (C) and/or (D) are electrophoretically separated using SDS-PAGE to determine the respective gene expression patterns.

44. (Amended) The method of Claim 42, wherein the protein(s) or glycoprotein(s) expressed in (A) and (B)[,] and/or (C) and/or (D) are electrophoretically separated using two-dimensional electrophoresis to determine the respective gene expression patterns.

45. (Amended) The method of Claim 29, wherein endocrine disruption is determined by identifying that a different amount of a protein or glycoprotein is expressed in the gene expression pattern of (A), compared to (B)[,] or (C) or (D).

46. (Amended) The method of Claim 29, comprising determining a variation in the amount of protein modification in said gene expression patterns, wherein a variation in protein modification between one or more proteins in the gene expression pattern of (A) compared to (B)[,] and/or (C) and/or (D) is indicative of an endocrine disrupting activity of the test substance.

47. (Amended) The method of Claim 46, where the variation in protein modification is measured by:

recovering the glycosylated proteins of (A), and (B)[,] and/or (C) and/or (D) by binding them to a substance that binds to a polysaccharide chain,
cleaving the polysaccharide chain from the glycoprotein, and
determining the gene expression patterns obtained from (A) and (B)[,] and/or (C) and/or (D) based on a comparison of the glycoproteins after cleavage.

48. (Unamended) The method of Claim 29, wherein said cell is a germ cell.

49. (Unamended) The method of Claim 29, wherein said cell is a nerve cell.

50. (Unamended) The method of Claim 29, wherein said cell is a normal cell.

51. (Unamended) The method of Claim 29, wherein said cell is a cancer cell.
52. (Unamended) The method of Claim 29, wherein said cell is a nonhuman mammalian cell.
53. (Unamended) The method of Claim 29, wherein said cell is a human cell.
54. (Unamended) The method of Claim 29, wherein said cell is not a genetically engineered cell.
55. (Unamended) The method of Claim 29, wherein said cell is selected from the group consisting of a murine neuroblastoma cell, a murine uterus carcinoma cell, a murine testicular Leydig cell, a cell derived from testicular Sertoli cells.
56. (Unamended) The method of Claim 29, wherein said cell is selected from the group consisting of Neuro2a, MCF7, TM3, TM4, 15P-1 and S-20Y.
57. (Unamended) The method of Claim 29, wherein said endocrine hormone is a female hormone.
58. (Unamended) The method of Claim 29, wherein said endocrine hormone is estrogen, estradiol, or progesterone.
59. (Unamended) The method of Claim 29, wherein said endocrine hormone is a male hormone.
60. (Unamended) The method of Claim 29, wherein said endocrine hormone is androgen, testosterone, or androsterone.
61. (Unamended) The method of Claim 29, wherein said endocrine hormone is an adrenal cortex hormone.
62. (Unamended) The method of Claim 29, wherein said endocrine hormone is cortisol, aldosterone, corticosterone or cortisone.

63. (Unamended) The method of Claim 29, wherein said endocrine hormone is an amino acid derivative hormone.

64. (Unamended) The method of Claim 29, wherein said endocrine hormone is triiodothyronine (T3), thyroxine (T4) or a parathyroid hormone.

65. (Amended) A method of detecting an endocrine disrupting action of a test substance, comprising:

(A) culturing a cell, which [that] has not been genetically engineered [that] and which is sensitive to an endocrine hormone, in the presence of the endocrine hormone and the test substance and detecting a gene expression pattern (1) of said cell; and

(B) culturing said cell, which has not been genetically engineered and which [that] is sensitive to an endocrine hormone, in the presence of the endocrine hormone, but in the absence of the test substance, and detecting a gene expression pattern (2) of said cell; and/or

(C) culturing said cell, which has not been genetically engineered and which [that] is sensitive to an endocrine hormone, in the absence of the endocrine hormone, but in the presence of the test substance, and detecting a gene expression pattern (3) of said cell; and/or

(D) culturing said cell, which has not been genetically engineered and which [that] is sensitive to an endocrine hormone, in the absence of the endocrine hormone and in the absence of the test substance, and detecting a gene expression pattern (4) of said cell; and

(E) comparing gene expression pattern (1) with gene expression pattern (2)[,] and/or (3) and/or (4) to determine the endocrine disrupting activity of the test substance, wherein the increased or decreased expression of a gene in expression pattern (1) compared to the same gene in expression pattern (2)[,] and/or (3) and/or (4) is indicative of endocrine disrupting action by the test substance.

Please add new Claims 66-69:

--66-69. (New)--